

Incidence Profile of Side Effects of Anti-Tuberculosis Drugs and Adherence To Taking Medication In Tuberculosis Patients At The Sukolilo 1 Health Center

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Abstract.

Tuberculosis (TB) is a disease caused by infection with the bacterium Mycobacterium tuberculosis and can be fatal. Long-term TB treatment has the potential to cause side effects, but adherence to medication is still necessary to achieve therapeutic effectiveness, reduce the risk of transmission, and prevent drug resistance. This study aims to determine the relationship between the side effects of anti-TB drugs (OAT) and medication adherence in TB patients at the Sukolilo Community Health Center in Pati. This study used a descriptive observational method with a cross-sectional approach. A total of 100 patients met the inclusion criteria: aged 18–65 years, making outpatient visits during August 2025, having at least two visits with a TB diagnosis, and willing to be research subjects. Respondents with incomplete questionnaires were excluded from this study. The study showed that the majority of patients were aged 61–65 years, male (64.0%), with the highest level of education being elementary school (48.0%), and working as farmers (60.0%). Most patients were married (87.0%) and had a family of four (40.0%). The most common side effect of OAT was joint pain (40.0%), while the least common were burning sensation in the feet and visual disturbances (5.0 each). The level of medication adherence was mostly in the moderate category (96.0%). The results showed no relationship between the side effects of OAT use and medication adherence in tuberculosis patients, with a p-value of 0.521.

Keywords: Tuberculosis, anti-TB drugs, side effects, medication adherence and Sukolilo 1 Community Health Center.

I. INTRODUCTION

Pulmonary TB is an infectious disease that falls into one of the categories of dangerous diseases and is one of the leading causes of death in the world. More than 1.6 million people with tuberculosis die every year. In 2019, the number of deaths of people with TB was around 1.4 and the number of deaths of people with TB increased in 2021, which was 1.6 million deaths every year. The prevalence of pulmonary TB patients in 2021 which occurred in the Southeast Asian continent was 45%, Africa 23%, the Western Pacific 18%, America 2.9% and Europe 2.2%. The Southeast Asian continent is the highest prevalence in the world, and the 3 countries with the highest burden in Southeast Asia are India, China, and Indonesia (WHO, 2022). Tuberculosis (TB) is currently a public health problem in the world. Pulmonary TB is ranked 2nd as the leading cause of death due to infectious diseases after Human Immunodeficiency Virus (HIV). (WHO, 2022). Tuberculosis is the ninth leading cause of death in the world. The number of TB cases in the world is 10.4 million and 45% of cases occur in the Southeast Asian region and 25% occur in the African region (Pusdatin of the Ministry of Health of the Republic of Indonesia, 2018 and the Ministry of Health of the Republic of Indonesia, 2018). In Indonesia, there are 824 thousand cases of people suffering from tuberculosis, the death rate of suffering from pulmonary TB disease reaches 93 thousand people every year. In 2022, Indonesian health workers managed to detect the latest cases of pulmonary TB as many as 700 thousand cases. Based on the 2023 Tuberculosis Report, the estimated number of TB cases has increased to 1,060,000 new cases per year. Then the death rate reached 134 thousand per year.

Treatment of tuberculosis is the most efficient effort to cure, reduce the spread of TB-causing bacteria, prevent death and drug resistance. Treatment of tuberculosis takes a relatively long time with two stages of treatment, namely the intensive stage and the advanced stage to avoid recurrence. Treatment must be adequate and generally drugs are given in the form of an anti-TB drug (OAT) combination that contains at least 4 types of drugs to prevent resistance. Treatment with a combination of medications can prevent resistance but may increase the likelihood of drug side effects. The side effects of the drug will affect the patient's adherence to taking the drug. Most patients who complain of mild and severe side effects often

choose to discontinue treatment because they are afraid that if the treatment is continued, it will get worse and they will not be able to tolerate it if they continue ($> \alpha 0.05$) (Ningsih, et al. 2022). The side effects of OAT are divided into two, namely mild side effects and severe side effects. Mild side effects: no appetite, nausea while severe side effects: abdominal pain, redness of urine, joint pain, fever chills and itching of the skin. Side effects of OAT are more common in the first and second weeks of treatment, so at the beginning of treatment the patient has begun to get bored and feel useless in taking treatment because instead of getting better, the disease is getting worse. According to Nugroho (2017) research, it is stated that OAT has side effects that can be felt by TB patients, side effects from OAT occur more at the beginning of treatment so that patients stop receiving treatment and as a result patients experience immunity to OAT or called Multi Drug Resistant (MDR TB) (Amining et al. 2021).

Compliance is very important especially in the treatment of tuberculosis, this is so that the treatment carried out can be effective. The success of TB treatment depends on the patient's adherence to treatment therapy. Discipline in obeying the rules of medicine is influenced by the behavior of the individual himself. There are three factors that affect individual behavior, namely, first, predisposing factors related to individual personality, education level and knowledge. The two factors may consist of drug side effects and drug availability and the third boosting factor is the staffing of health workers, family support and drug supervisory officers (PMOs). Compliance can be interpreted as the patient's behavior to obey all the rules and instructions recommended by health workers. In achieving recovery, patients must obediently take the medicines prescribed by the doctor at the right time and dosage (November 2023).

According to Sulaiman & Dawu, the results are that many severe side effects are not compliant in taking medication, because the severity of the side effects felt by patients in taking TB drugs results in higher non-compliance with taking TB drugs. Furthermore, the results of Tobing's (2024) research, drug side effects affect the compliance of pulmonary TB patients in taking drugs at the Batang Beruh Health Center UPT, Sidikalang District, Dairi Regency. Judging from the results of the statistical test *Chi-Square* Significant results were obtained $p=(0.000)$ or (<0.05) so that it can be concluded that there is a relationship between side effects and medication adherence of TB patients in the working area of the Tumbu-Tumbu Jaya Health Center. The results of this study are in line with the research conducted by Wulandari (2015), stating that there is a significant relationship ($p = 0.000$) between OAT side effects and medication adherence to pulmonary TB patients. This means that TB patients who have mild side effects tend to be compliant by 22.3 times more than patients who experience severe side effects (Sulaiman and Dawu 2024).

This is different from Sophia Fitriani's research, there is no significant relationship between OAT side effects and treatment adherence of Pulmonary Tuberculosis patients in Sungai Kunjang District. According to research (Zukhrufina Muthiah Nabilah, Widiastuti, and Ayu Nissa Ainni 2024) There was no significant association between OAT side effects and medication adherence from the value of the *p-value* by $0.737 > 0.05$. The purpose of this study was to analyze the relationship between the incidence of mild and severe side effects of anti-tuberculosis drug use and medication adherence in tuberculosis patients.

II. METHODS

This research was conducted in August 2025 at the Sukolilo 1 Health Center, Sukolilo District, Pati Regency, Central Java. The research method used was descriptive observational with a *cross sectional approach*. Sampling was carried out using *purposive sampling* techniques. The inclusion criteria set are patients aged 18 - 65 years, have received outpatient services since the beginning of treatment and have been diagnosed with tuberculosis in the August 2025 period, have made at least two medical visits, are willing to be respondents, and are able to read and write. The diagnosis of tuberculosis is confirmed from the patient's medical records. The exclusion criteria in this study were patients who did not fill out the questionnaire completely.

The instruments used in measuring medication adherence were the *MARS* 5 questionnaire with a low compliance category with a score of 5, moderate compliance with a score of 6-24 and high compliance with a value of 25 and above. The Adverse Effects Assessment Instrument is a list of questions about side effects containing 11 questions felt by patients during TB treatment. Respondents were given a choice of "Yes" or

"No" answers to each question. No: 0 (if there are no side effects) and Yes: 1 (if there are side effects). Adverse *Drug Reaction* or side effect analysis is carried out by calculating scores from filling out question sheets collected from patients. The calculation of the incidence of side effects was carried out by the percentage of the incidence of drug side effects in patients compared to the number of all patients. This research received ethical approval from the Health Research Ethics Committee of the University of Muhammadiyah Purwokerto (KEPK-UMP) with the number KEPK/UMP/151/VII/2025.

The sample consisted of 100 patients who had undergone outpatient treatment at the Sukolilo 1 Health Center. The inclusion criteria set are patients aged 18 - 65 years, have received outpatient services since the beginning of being diagnosed with TB and are undergoing treatment, have made at least two visits after being diagnosed with TB in the August 2025 period, are willing to be respondents, and are able to read and write. The exclusion criteria in this study were patients who did not fill out the questionnaire completely. Patients are instructed to fill out a questionnaire as a respondent which takes about 10-15 minutes. After respondents complete the questionnaire, the data is recorded in a table, grouped, and analyzed. The data analysis method of this study is univariate and bivariate analysis.

III. RESULT AND DISCUSSION

Respondent Characteristics

Here is a table of the results of the respondents' characteristics. This data was collected from 100 respondents who answered the question.

Table 1. Frequency distribution based on respondent characteristics at the Sukolilo 1 Health Center

Age	Frequency	Present %
18-30	19	19,0%
31-40	15	15,0%
41-50	20	20,0%
51-60	21	21,0%
61-65	25	25,0%
Gender	Frequency	Present %
Male	64	64%
Women	36	36,0%
Education	Frequency	Present %
SD	48	48,0%
Junior High School	17	17,0%
High School	35	35,0%
Jobs	Frequency	Present %
Farmer	60	60,0%
Self-employed	30	30,0%
PNS	10	10,0%
Marital Status	Frequency	Present %
Married	87	87,0%
Unmarried	13	13,0%
Number of Families	Frequency	Present %
2	7	7,0%
3	24	24,0%
4	40	40,0%
5	29	29,0%
Quantity	100	100%

According to table 1, it can be seen that out of 100 respondents, the majority of patients are in the age group of 61-65 years, with the largest gender being 64 men (64.0%), with an elementary education level of 48 people (48.0%), the majority of whom work as farmers as many as 60 orang (60.0%), with married marriage status 87 people (87.0%), with a total of 4 families of 40 people (40.0%).

Table 2. Drugs Given to Tuberculosis Patients

Weight	Intensive Stage RHZE	Amount of RHZE used (Tablet)	Advanced Stage RH	Number of RH used (Tablet)
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30-37 kg	2 Tablets 4KDT	112	2 Tablets 2 KDT	192
38-45 kg	Tablets KDT	168	3 Tablets 2 KDT	288
55-70 kg	Tablets 4 KDT	224	4Tablet 2 KDT	384
71 kg	Tablets 4 KDT	280	Tablets 2 KDT	480

Description :

The drug consists of

1. 2 months early: Isoniazid (H), Rifampicin (R), Pyrazimide (Z), and Ethambutol (E) for 2 months in the early stages.
2. 4 months follow-up: Isoniazid (H), and Rifampicin (R).

The number of OAT tablets is given to each patient according to the weight recommended by the doctor.

Characteristics of Side Effects and Compliance of Tuberculosis Patients

Data on side defects felt by tuberculosis patients using OAT during treatment.

Table 3. Overview of Side Effects

Yes	Side Effects	Remarks	Frequency	Percentage %
1	Reddish Urine	Yes	34	34,0%
		No	66	66,0%
		Total	100	100%
2	Nausea	Yes	31	31,0%
		No	69	69,0%
		Total	100	100%
3	No Appetite	Yes	28	28,0%
		No	72	72,0%
		Total	100	100%
4	Joint Pain	Yes	40	40,0%
		No	60	60,0%
		Total	100	100%
5	Abdominal Pain	Yes	47	47,0%
		No	53	53,0%
		Total	100	100%
6	Fever	Yes	27	27,0%
		No	73	73,0%
		Total	100	100%
7	Shivering	Yes	35	35,0%
		No	65	65,0%
		Total	100	100%
8	Tingling	Yes	41	41,0%
		No	59	59,0%
		Total	100	100%
9	Reddish Skin	Yes	15	15,0%
		No	85	85,0%
		Total	100	100%
10	Burning sensation in the legs	Yes	5	5,0%
		No	95	95,0%

		Total	100	100%
11	Vision Impairment	Yes	5	5,0%
		No	95	95,0%
		Total	100	100%

Based on table 3, it was found that several side effects experienced by respondents during treatment. A total of 34 people (34.0%) experienced reddish urine, while 66 people (66.0%) did not. Side effects in the form of nausea were experienced by 31 respondents (31.0%) and not experienced by 69 respondents (69.0%). In addition, 28 respondents (28.0%) reported no appetite, while 72 respondents (72.0%) did not feel it. Joint pain is one of the most common complaints, experienced by 40 respondents (40.0%), while 60 respondents (60.0%) do not experience it. Abdominal pain was experienced by 47 respondents (47.0%) and not experienced by 53 respondents (53.0%). Fever was found in 27 respondents (27.0%), while 73 respondents (73.0%) did not experience it. Shivers were experienced by 35 respondents (35.0%) and not experienced by 65 respondents (65.0%). A total of 41 respondents (41.0%) reported tingling, while 59 respondents (59.0%) did not feel it. Redness of the skin was only experienced by 15 respondents (15.0%), while the majority, namely 85 respondents (85.0%), did not experience it. Side effects in the form of burning in the legs and visual impairment were the least, each experienced by only 5 respondents (5.0%), while 95 respondents (95.0%) did not feel these symptoms

Table 4. Characteristics of mild and severe side effects

Mild Side Effects	Severe Side Effects
Reddish urine (The cause of red urine in tuberculosis patients after consuming OAT is the metabolic process of the drug Rifampicin) (Sukarno et al. 2023)	Redness of the skin (Medications such as Rifampicin and Pirazinamide often cause side effects on the skin in the form of red, dry, and itchy skin. Both can also improve the skin's sensitivity to sunlight. Rifampicin itself is reported to cause darker skin discoloration, but this effect includes rare effects)
Nausea (Increased stomach acid due to certain medications, such as isoniazid and rifampicin) (Ministry of Health 2020)	Burning sensation in the legs (This condition is a side effect of OAT, i.e. <i>isoniazid</i> . The drug can cause damage to peripheral nerves (neuropathy), resulting in tingling and burning symptoms, especially at the ends of the limbs. Under certain conditions, the use of <i>isoniazid</i> does not need to be stopped and the doctor will give an additional intake of B vitamins)
No appetite (TB patients who have just started taking OAT will usually experience gastrointestinal side effects, such as reduced appetite.)	Vision Impairment (Every patient who receives Etambutol should be reminded that if symptoms of vision impairment occur, eye examination should be done immediately. Vision impairment will return to normal within a few weeks after the medication is stopped.) (Chandra Mohapatra et al., 2021).
Joint pain (One of the OATs that can cause joint pain is pirazinamide. (Chandra Mohapatra et al., 2021).	

Table 5. Overview of Medication Compliance

Compliance with Anti-Tuberculosis Medication	Frequency	Percentage %
Low Compliance	0	0,0%

Moderate Compliance	96	96,0%
High Compliance	4	4,0%
Quantity	100	100%

Based on table 5, it can be seen that the level of adherence to taking anti-tuberculosis drugs in respondents is mostly in the medium category, which is as many as 96 respondents (96.0%). Only 4 respondents (4.0%) had high compliance, and no respondents were found with low compliance (0.0%). This illustrates that the majority of TB patients are quite consistent in taking medication, although it is not completely optimal.

Relationship of the incidence of mild and severe side effects with medication adherence of tuberculosis patients

The following data presents the distribution of the incidence of OAT side effects with medication adherence to TB patients at the Sukolilo 1 Health Center. Here is a table detailing those relationships

Table 6. The Relationship between the Incidence of Side Effects of Anti-Tuberculosis Drug Use (OAT) and Medication Adherence in Tuberculosis Patients.

MARCH 5									
	Low compliance		Moderate Compliance		High Compliance		Total		
MARCH 5	n	%	n	%	N	%	N	%	P value
Lightweight	0	0,0	87	87,0	4	4,0	91	91,0	0,521
Weight	0	0,0	9	9,0	0	0,0	9	9,0	
Total	0	0,0	96	96,0	4	4,0	100	100,0	

Based on table 6, it is known that of the 100 respondents of tuberculosis patients who used anti-tuberculosis drugs, most of them experienced mild side effects, namely 91 people (91.0%), while 9 people (9.0%) experienced severe side effects. In the group with mild side effects, 87 people (87.0%) had moderate adherence and 4 people (4.0%) had high adherence. Meanwhile, in the group with severe side effects, as many as 9 people (9.0%) showed moderate adherence and none had high or low adherence. Overall, the majority of respondents had a moderate compliance rate of 96 people (96.0%) and only 4 people (4.0%) had high compliance, with no one having low compliance. The results of the statistical test showed a value of $p = 0.521$ which means that there was no significant relationship between the incidence of side effects of the use of anti-tuberculosis drugs and medication adherence in tuberculosis patients.

IV. DISCUSSION

The results of the study were obtained at the average age of those who experienced Pulmonary TB, namely at the age of 61-65 years (elderly). This is because the group that steps on the elderly is vulnerable to a decrease in the body's immunity along with the aging process so that the germs that enter cannot be overcome with decreased immunity.

The highest percentage of respondents obtained the highest percentage of respondents, namely respondents with elementary education (48.0%). From the data obtained, the majority of respondents are less educated. These results are the same as the research conducted by (Absorb *et al.* 2020) In his research, the level of elementary education was greater than others. This is because, the majority of sufferers are rural people whose average job is a farmer, trader, and fisherman who is only an elementary school graduate. Their motivation in learning is very low because of the demands in terms of the economy and the surrounding environment which also affect. Likewise, those who only graduate to junior high school and high school, apart from lack of motivation to learn, costs are also a reason not to continue to the next level of education. This is one of the factors of compliance in treatment, especially affecting their knowledge in carrying out treatment. The more individuals have a higher level of education, the more they will realize that health is an important thing for life so that they are motivated to visit better health care centers. Other research results that show risk factors that cause medication adherence are by Adam (2020) about the knowledge of Pulmonary Tuberculosis patients to the adherence to taking anti-tuberculosis drugs, it was

found that there is a relationship between knowledge and medication adherence. Education is embraced to get certain information to improve the quality of life, the higher a person's education, the easier it will be to receive information. This shows that Pulmonary Tuberculosis patients with a mostly educational background are in low education, so there may be a lack of attention to get information about the disease suffered or lack motivation in finding out about pulmonary tuberculosis.

In table 2, it can be seen that side effects are almost felt by all patients with tuberculosis. One of the side effects felt by patients is joint pain. In line with previous research theories, this happens because the drugs given and consumed have very strong side effects that cause joint pain in patients after consuming them. One of the OATs that can cause joint pain is pyrazinade (*Chandra Mohapatra et al., 2021*). Another side effect is reduced vision caused by Etambutol which can cause visual impairment in the form of reduced visual acuity, color blindness to red and green colors. However, the poisoning depends on the ocular on the dose used. Every patient who receives Etambutol must be reminded that if symptoms of vision impairment occur, an eye examination should be carried out immediately. Vision loss will return to normal within a few weeks after the medication is stopped.

Another side effect complained by patients is itching on the skin. Side effects in the form of itching and redness in the skin are not experienced by all patients because this depends on the sensitivity of the patient's skin. Itching in patients due to the use of OAT will usually disappear immediately with the administration of antihistamines. The treatment carried out by the Sukolilo Health Center is to provide antihistamines such as cetirizine to patients who experience itching complaints. In line with research (*Rosdianah et al. 2022*) which shows that the itchy side effects felt by the patient may be caused by an allergic reaction that arises after consuming the drug, so the management given is in the form of additional CTM without stopping the previous treatment.

In the event of side effects, it is quite difficult to determine which OAT is the cause. Therefore, it is better if the side effects/unwanted events are still in the mild category, they can be overcome by administering symptomatic drugs such as anti-nausea, anti-vomiting, antipyretic analgesics and vitamin B6. If the patient experiences severe side effects, it is necessary to consider replacing it with another drug. Treatment of side effects must be carried out continuously in TB patients. In this case, communication to health workers and the public is needed in order to increase the rational use of drugs so as to minimize the risk of drug side effects.

In table 3, it can be seen that tuberculosis patients have moderate (96.0%) and high compliance rates (4.0%). Adherence to medication reflects complex human behavior and can be influenced by many factors, such as factors related to the patient, health system, condition, therapy, and socioeconomic factors (*Sazali, 2023*).

Based on the results of the study on the relationship between side effects and medication adherence to TB patients, the results of the statistical test were $P=0.521$ which means that there was no relationship between side effects and medication adherence in TB patients. The research assumption why there is no relationship between drug side effects and medication adherence is because drug side effects are not a triggering factor that affects all patients or respondents to not comply with taking medication, this is supported by data in the form of medication adherence questionnaires where some respondents still forget to take medication and change the dose of taking medication. According to the researcher, this respondent's answer occurred because of a lack of understanding of the benefits of tuberculosis medicine and how tuberculosis can be cured or because of more trust in traditional medicine. Other things can also be caused by accident, meaning that the sufferer's non-compliance is accidentally caused by factors beyond the patient's control. Where the patient basically wants to obey all treatment instructions. The main factor that causes accidental non-compliance is that patients forget to take medication due to busy work or due to reduced memory as happens to elderly patients.

IV. CONCLUSION

The results of the study were obtained that the side effects that are often felt by tuberculosis patients are abdominal pain 47% and joint pain 40%. The results of the study obtained the most moderate

compliance, which was 96% and high compliance of 4% The results of the analysis test obtained a p value of 0.521 , so it can be concluded that there is no strong relationship between the side effects of Pulmonary Tuberculosis drugs and adherence to taking anti-tuberculosis drugs in Pulmonary TB patients at the Sukolilo 1 Health Center UPT.

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